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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH ENDOTHELIAL DIFFERENTIATION, SPHINGOLIPID G-PROTEIN-COUPLED RECEPTOR 6(EDG6)

(57) Abstract: The invention provides a human EDG6 which is associated with the cardiovascular disorders, gastrointestinal and liver diseases, inflammatory diseases, hematological disorders, respiratory diseases, neurological disorders, urological disorders, thrombocytopenia and myeloma. The invention also provides assays for the identification of compounds useful in the treatment or prevention of cardiovascular disorders, gastrointestinal and liver diseases, inflammatory diseases, hematological disorders, respiratory diseases, neurological disorders, urological disorders, thrombocytopenia and myeloma. The invention also features compounds which bind to and/or activate or inhibit the activity of EDG6 as well as pharmaceutical compositions comprising such compounds.



### INTERNATIONAL SEARCH REPORT

International Ilication No
PCT/EP2004/002731

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/566

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) I PC  $\,\,7\,$  GO1N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, Sequence Search

ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
•	DATABASE AAGENESEQ 4 March 2003 (2003-03-04), XP002307015 Database accession no. ABP82007 Document cited to provide information on the relevant sequence disclosed in W0-A-02/61087 abstract	19-26
(	& WO-02/061087 A (ROUSH CHRISTINE L; BROWN JOSEPH P (US); BURMER GLENNA C (US); LIFESPA) 8 August 2002 (2002-08-08) Seq Id No 502.	19-26
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Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.			
Special categories of cited documents:      "A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention			
"E" earlier document but published on or after the international filing date  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "P" document published prior to the international filing date but later than the priority date claimed	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family			
Date of the actual completion of the international search 23 November 2004	Date of mailing of the international search report  1 9. 04. 2005			
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016	Authorized officer  Luis Alves, D			

## INTERNATIONAL SEARCH REPORT

international lication No
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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>		
		Relevant to claim No.		
Category °	Citation of document, with indication, where appropriate, or the rotoral passages			
Х	PYNE S ET AL: "REVIEW ARTICLE SPHINGOSINE 1-PHOSPHATE SIGNALLING IN MAMMALIAN CELLS" BIOCHEMICAL JOURNAL, THE BIOCHEMICAL SOCIETY, LONDON, GB, vol. 349, 2000, pages 385-402, XP000939036 ISSN: 0264-6021	19-26		
A	abstract page 397, right-hand column, paragraph 3 - page 398, left-hand column, paragraph 3	1-18		
X	RACKE K ET AL: "Potential role of EDG receptors and lysophospholipids as their endogenous ligands in the respiratory tract"	19-26		
	PULMONARY PHARMACOLOGY AND THERAPEUTICS, ACADEMIC PRESS, NEW YORK, NY, US, vol. 13, no. 3, 2000, pages 99-114, XP002277298 ISSN: 1094-5539 abstract page 109, left-hand column, paragraph 3 - right-hand column, paragraph 1; table 1			
X	GRAELER M H ET AL: "Cellular functions of the lymphoid-specific sphingosine 1-phosphate binding receptor EDG6" IMMUNOBIOLOGY, vol. 203, no. 1-2, November 2000 (2000-11), page 111, XP009039072 & JOINT ANNUAL MEETING OF THE GERMAN AND DUTCH SOCIETIES OF IMMUNOLOGY; DUSELDORF, GERMANY; NOVEMBER 29-DECEMBER 02, 2000 ISSN: 0171-2985 abstract	19-26		
L	DATABASE AAGENESEQ 29 July 2004 (2004-07-29), XP002307016 Database accession no. AD029295 Document cited to provide information on the relevant sequence disclosed in W02004/040000	1-26		
Е	abstract & WO 2004/040000 A (GAITANARIS GEORGE A; MCILWAIN KELLIE L (US); MADISEN LINDA (US); BERG) 13 May 2004 (2004-05-13) page 7 - page 8; claims 37-42; tables 6,7	1-26		

## INTERNATIONAL SEARCH REPORT



Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)					
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:					
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  Although claim 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.					
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:					
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).					
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)					
This International Searching Authority found multiple inventions in this international application, as follows:					
see additional sheet					
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.					
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.					
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:					
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-26 (all partially)					
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.					

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of Alzheimer's and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

2. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of spleen (liver?) cirrohsis (?) and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

3. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of ileum chronic inflammation and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

4. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of liver cirrohsis and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

5. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of lung COPD and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

6. claims: 1-26 (all partially)

Methods of screening for therapeutical agents useful in the treatment of prostate tumour and methods of diagnosing said disease using as target EDG6, as well as pharmaceutical compositions comprising EDG6 polynucleotide or polypeptide.

## INTERNITIONAL SEARCH REPORT

Information on patent family members

Internationa Ilication No PCT/EP2004/002731

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 02061087	Α	08-08-2002	MO	02061087	A2	08-08-2002
WO 2004040000	Α	13-05-2004	AU WO	2003300776 2004040000		25-05-2004 13-05-2004